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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/806,368	09/20/2001	Mieko Katsuura	447.001	8538

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EXAMINER

HUNNICUTT, RACHEL KAPUST

ART UNIT	PAPER NUMBER
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1647

DATE MAILED: 02/03/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/806,368

Applicant(s)

KATSUURA ET AL.

Examiner

Rachel K. Hunnicutt

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 14 September 2004 and 19 October 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-18 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 16 and 18 is/are allowed.
- 6) ☒ Claim(s) 1-15 and 17 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

RESPONSE TO AMENDMENT

Applicant's amendment filed September 14, 2004 and the supplemental amendment filed October 19, 2004 are acknowledged. Claim 1 is amended. Claims 16-18 are new. Claims 1-18 are under consideration. The text of those sections of Title 35, U.S. Code, not included in this action can be found in a prior office action.

Claim Rejections/Objections Withdrawn

The objection to the specification regarding the use of trademarks is withdrawn in response to Applicant's amendments to the specification.

The rejection of claims 1, 2, 4, 5, 8, and 12-15 under 35 U.S.C. 112, first paragraph, as not being enabled for MP52 proteins modified at residue 111, is withdrawn in response to Applicant's amendment to the claims.

Claim Rejections/Objections Maintained and New Grounds of Rejection***Claim Rejections - 35 USC § 112***

The rejection of claims 1-15 under 35 U.S.C. 112, first paragraph, as not being enabled for modified BMPs (MP52, BMP-2, BMP-4, or BMP-7) that act as antagonists against any BMP, is maintained for reasons of record on p. 3 of paper no. 0604 and is applied to new claim 17.

Applicants argue that BMPR-1 (a and b) and BMPR-II receptors play a critical role in bone formation, that both types are necessary for signal transduction, and if one of the two receptor types is not available for signal transduction, then there will be no signal transduction (p. 10 of the response). Thus, Applicants argue that when a modified MP52 binds to the BMPR-II receptor, none of the other BMPs such as BMP-2, BMP-4 or BMP-7 would be able to bind to BMPR-II and signal transduction would not be induced.

Applicant's arguments have been fully considered but have not been found to be persuasive. Claims 1-8, 12-15, and 17 encompass modified MP52 proteins which have an antagonistic activity against all BMPs. Claims 9-11 encompass modified BMP-2,

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BMP-4, and BMP-7 proteins which have an antagonistic activity against all BMPs. In the response, Applicants state that MP52 bind to the BMPR-II receptor and it binds preferably to BMPR-Ib and not BMPR-Ia (p. 10). However, Massagué teaches that ActR-II and IIb can bind BMPs 2 and 7 in cooperation with BMPR-Ia or Ib (1998, *Annu. Rev. Biochem.* 67: 753-791, see p. 762). Thus, even if the modified MP52 is binding BMPRII and BMPR-Ib, BMPs 2 and 7 can still induce signal transduction by binding to ActR-II or Ib and BMPR-Ia. As stated in paper no. 0604 on p. 3, the members of the BMP family show different affinities to the different combinations of type I and type II receptors. One skilled in the art would not be able to use a modified MP52, BMP-2, BMP-4 or BMP-7 such that the protein is an antagonist against all BMPs because of the different affinities of each protein to the different combinations of receptors.

The rejection of claims 1-15 under 35 U.S.C. 112, first paragraph, for failing to comply with the written description requirement, is maintained for reasons of record on p. 3-4 of paper no. 0604 and is applied to new claim 17.

Applicants argue that examples in the specification show that a mature modified MP52 is not only active as an antagonist against MP52 but also against BMP-2. MP52, BMP-2, BMP-4, and BMP-7 all bind to BMPR-II, and Applicants argue that the modified MP52 would have the same antagonistic activity against other BMPs since they all use the same general mechanism (p. 12 of response).

Applicant's arguments have been fully considered but have not been found to be persuasive. As stated above, even if the modified MP52 is binding BMPRII and BMPR-Ib, BMPs 2 and 7 can still induce signal transduction by binding to ActR-II or ActRIb and BMPR-Ia. Applicants are claiming polypeptides which are antagonists against all BMPs, and Applicants have not conveyed to one skilled in the relevant art that they were in possession of the claimed invention.

Claims 12-15 are newly rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to

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which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 12 and 13 are drawn to modified MP52 polypeptides which can be used in the treatment and/or prevention of ectopic ossification or metabolic diseases with calcification. Claims 14 and 15 drawn to methods of treating ectopic ossification or metabolic diseases with calcification by administering modified MP52 polypeptides. One skilled in the art would not know how to make and/or use the invention as it is claimed. In order for the modified MP52 polypeptides to be effective in treating a disease, the disease must be due to an over-abundance of BMPs and BMPR-II must be the receptor involved in the disease. This limitation, however, is not in the claims, and one skilled in the art would not know how to use the claimed invention otherwise. In addition, some of the diseases encompassed by the claims are due to congenital defects such as genetic mutations in the BMPR-II receptor which destroy the activity of the receptor (see, for example Strange *et al.* (2002), *Clinical Science* 102: 253-268). One skilled in the art could not use the invention as claimed to prevent these diseases, as such genetic diseases are not preventable. One skilled in the art could also not use the invention as claimed to treat such diseases, because an antagonist that binds to a non-functioning receptor would have no therapeutic effect. Thus, the invention is not enabled as claimed.

Conclusion

Claims 16 and 18 are allowed.

Claims 1-15 and 17 are rejected.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rachel K. Hunnicutt whose telephone number is (571) 272-0886. The examiner can normally be reached on Mon-Fri 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on (571) 272-0961. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

RKH
2/1/05


JANET ANDRES
PRIMARY EXAMINER